

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 3 -

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 (original): A method of preparing an amine stereoisomer, which comprises stereoselectively reducing a sulfinylimine that bears on the sulfinyl group a residue of an alcohol, thiol or amine, or reacting a sulfinylimine stereoisomer that bears on the sulfinyl group a residue of an alcohol, thiol or amine with a source of a nucleophile, to afford a sulfinylamine stereoisomer, followed by contacting the sulfinylamine stereoisomer with a reagent suitable for the cleavage of a sulfur-nitrogen bond, to afford an amine stereoisomer.

2 (original): A method as claimed in Claim 1, wherein the sulfinylimine is a sulfinylimine stereoisomer.

3 (previously presented): A method as claimed in Claim 1, wherein the residue of the alcohol, thiol or amine is in stereoisomeric form.

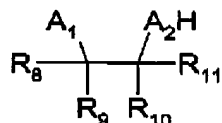
4 (previously presented): A method as claimed in Claim 1, wherein the residue of the alcohol, thiol or amine is a residue of an optionally N-substituted beta-amino alcohol, thiol or amine.

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 4 -

5 (original): A method as claimed in Claim 4, wherein the optionally N-substituted beta-amino alcohol, thiol or amine is a compound of the general formula



wherein  $\text{A}_1$  is  $\text{R}_7\text{N}$  or  $(\text{R}_{7'})\text{R}_{7''}\text{N}$ ,  $\text{R}_7$  represents hydrogen or  $-\text{L}-\text{R}_{7a}$  in which  $-\text{L}-$  represents a bond,  $-\text{CO}-$ ,  $-(\text{CO})\text{O}-$ ,  $-(\text{CO})\text{NR}_{7b}-$ ,  $-\text{SO}-$ ,  $-\text{SO}_2-$ , or  $-(\text{SO}_2)\text{O}-$ , each of  $\text{R}_{7a}$  and  $\text{R}_{7b}$  independently represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, and  $\text{R}_{7'}$  and  $\text{R}_{7''}$  are as defined for  $\text{R}_{7a}$ , or  $\text{R}_{7'}$  and  $\text{R}_{7''}$  together with the nitrogen atom to which they are attached and, optionally  $\text{R}_8$ , form an unsubstituted or substituted heterocyclic group, or  $\text{R}_{7'}$  together with the nitrogen atom to which it is attached and the carbon atom to which the nitrogen atom is attached forms an unsubstituted or substituted heterocyclic group;  $\text{A}_2$  is O, S or  $\text{NR}_{7c}$  in which  $\text{R}_{7c}$  is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and each of  $\text{R}_8$ ,  $\text{R}_9$ ,  $\text{R}_{10}$  and  $\text{R}_{11}$  is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or  $\text{R}_8$  and  $\text{R}_{11}$  together form a substituted or unsubstituted alkylene or heteroalkylene chain.

6 (original): A method as claimed in Claim 5, wherein  $\text{A}_2$  is O.

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 5 -

7 (previously presented): A method as claimed in Claim 5, wherein each of  $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  is independently selected from hydrogen, (1-4C)alkyl and phenyl, or the alcohol is selected from (N-methylpyrrolidin-2-yl)diphenylmethanol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

8 (original): A method as claimed in Claim 7, wherein  $A_1$  is  $R_7N$  wherein  $R_7$  represents  $-SO_2-R_{7a}$  in which  $R_{7a}$  represents (1-6C)alkyl, (6-10C)aryl(1-4C)alkyl or (6-10C)aryl in which any aryl group is unsubstituted or substituted by one, two or three substituents selected independently from halogen, (1-4C)alkyl and (1-4C)alkoxy, or  $A_1$  is  $(R_{7'})R_{7''}N$  wherein  $R_{7'}$  and  $R_{7''}$  each independently represents a (1-4C)alkyl group or together with the nitrogen to which they are attached represent a pyrrolidine group that may bear one or two methyl substituents, or the alcohol is selected from (N-methylpyrrolidin-2-yl)diphenylmethanol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

9 (original): A method as claimed in Claim 7, wherein  $A_1$  is  $R_7N$  and the residue of the alcohol, thiol or amine is a residue of an optionally N-substituted 2-amino-1-phenylpropanol, 2-amino-2-methyl-1-phenylpropanol, 1-amino-1-phenyl-2-propanol, 1-amino-1-phenyl-2-methyl-2-propanol, 1-amino-1-phenyl-2-ethyl-2-butanol, 1-amino-2-indanol, 2-aminoindan-1-ol, 1-amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene or 2-amino-1-hydroxy-1,2,3,4-tetrahydronaphthalene, or  $A_1$  is  $(R_{7'})R_{7''}N$  and the alcohol is selected from 2-N,N-dimethylamino-1-phenyl-2-propanol, 2-N,N-

Serial No. 10/508,941

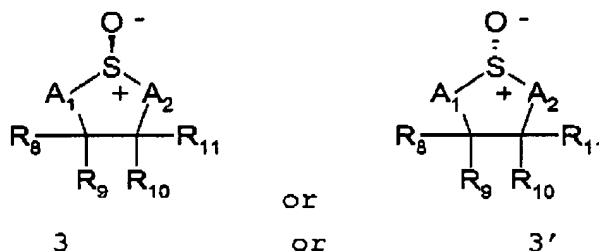
Response to Office Communication of December 15, 2005

- 6 -

dibutylamino-1-phenylpropanol, 2-pyrrolidin-1-yl-1-phenylpropanol, 2-(2-methylpyrrolidin-1-yl)-1-phenylpropanol, 2-(2,5-dimethylpyrrolidin-1-yl)-1-phenylpropanol, 2-N,N-dimethylamino-2-methyl-1-phenylpropanol, (N-methylpyrrolidin-2-yl)diphenylmethanol, 1-pyrrolidin-1-ylindan-2-ol, 3-benzyloxy-2-N,N-dimethylamino-1-phenylpropan-2-ol, quinine, quinidine, hydroquinine, cinchonidine, cinchonine, hydrocinchonidine and ethyl hydrocupreine.

10 (previously presented): A method as claimed in Claim 4, wherein the sulfinylimine has been prepared by contacting an iminometal with a 1,2,3-oxathiazolidine-S-oxide, a 1,2,3-dithiazolidine-S-oxide or a 1,2,3-azathiazolidine-S-oxide.

11 (previously presented): A method as claimed Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide is a compound of formula 3 or 3'



wherein  $A_1$  is  $R_7N$  or  $(R_{7'})R_{7''}N^+Q^-$  in which  $Q^-$  is an anion,  $R_7$  represents hydrogen or  $-L-R_{7a}$  in which  $-L-$  represents a bond,  $-\text{CO}-$ ,  $-(\text{CO})\text{O}-$ ,  $-(\text{CO})\text{NR}_{7b}-$ ,  $-\text{SO}-$ ,  $-\text{SO}_2-$ , or  $-(\text{SO}_2)\text{O}-$ , each of  $R_{7a}$  and  $R_{7b}$  independently represents substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, and  $R_{7'}$  and  $R_{7''}$  are as defined for  $R_{7a}$ , or  $R_{7'}$  and  $R_{7''}$  together with the nitrogen

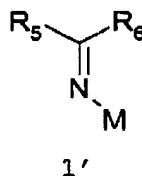
Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 7 -

atom to which they are attached and, optionally  $R_8$ , form an unsubstituted or substituted heterocyclic group, or  $R_7$ , together with the nitrogen atom to which it is attached and the carbon atom to which the nitrogen atom is attached forms an unsubstituted or substituted heterocyclic group;  $A_2$  is O, S or  $NR_{7c}$  in which  $R_{7c}$  is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; and each of  $R_8$ ,  $R_9$ ,  $R_{10}$  and  $R_{11}$  is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or  $R_8$  and  $R_{11}$  together form a substituted or unsubstituted alkylene or heteroalkylene chain;

the iminometal is a compound of formula 1'



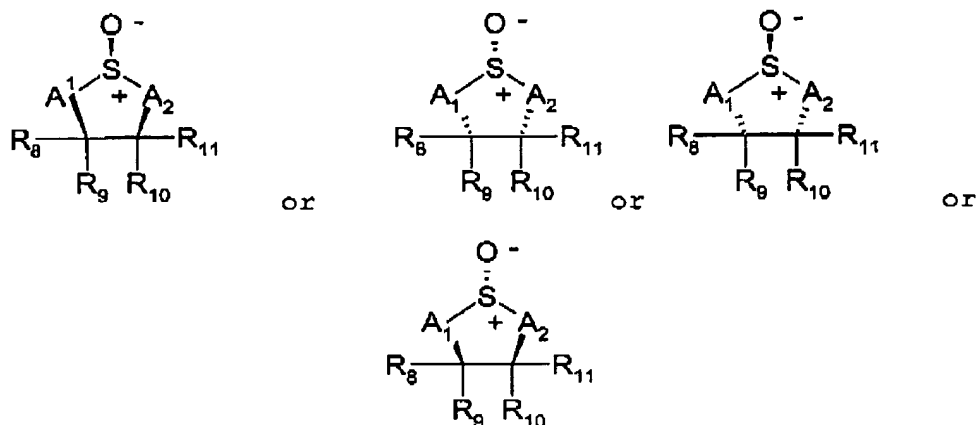
wherein M is  $CdZ$ ,  $BaZ$ , Na, K,  $MgZ$ ,  $ZnZ$ , Li,  $MnZ$ ,  $CuZ$ ,  $TiZ_3$  or In and Z is an anion.

12 (previously presented): A method as claimed in Claim 11, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide is a stereoisomer of formula

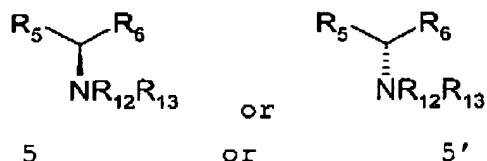
Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 8 -



13 (previously presented): A method as claimed in Claim 11, wherein the amine stereoisomer is a compound of formula 5 or 5'



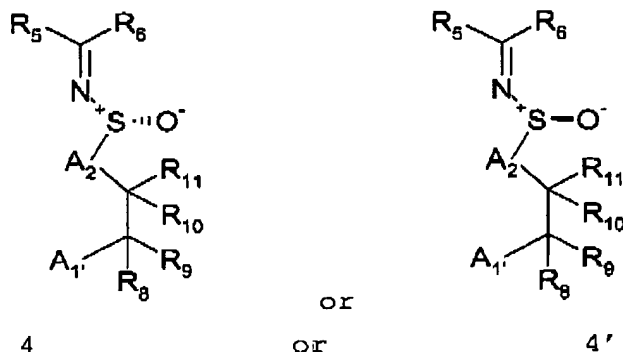
or a pharmaceutically acceptable salt, solvate, clathrate, hydrate or prodrug thereof, wherein R<sub>5</sub> and R<sub>6</sub> are independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl, or R<sub>5</sub> and R<sub>6</sub> together with the carbon atom to which they are attached form a substituted or unsubstituted cycloalkyl group, and R<sub>12</sub> and R<sub>13</sub> together with the nitrogen atom to which they are attached form a heterocycle, or each of R<sub>12</sub> and R<sub>13</sub> is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aryl;

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 9 -

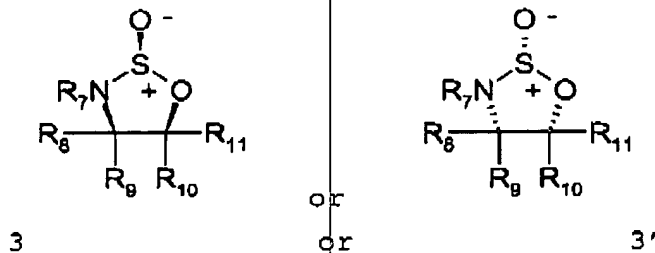
and the sulfinylimine stereoisomer is a compound of formula 4 or 4'



wherein  $A_1$  represents  $R_7N$  or  $(R_7)R_7N$ .

14 (original): A method as claimed in Claim 13, wherein  $A_2$  is O.

15 (original): A method as claimed in Claim 14, wherein  $R_5$  and  $R_6$  are independently substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl; the 1,2,3-oxathiazolidine-S-oxide is a compound of the formula 3 or 3'



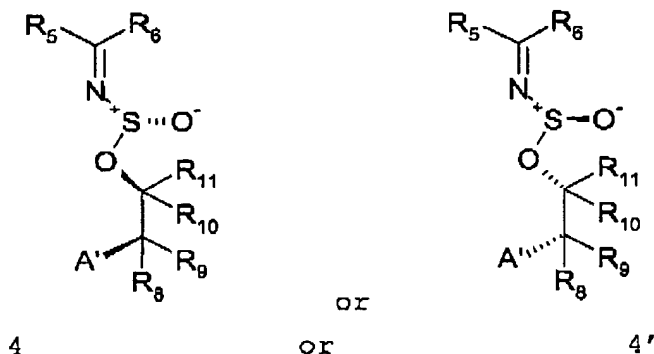
in which  $R_7$  represents hydrogen or  $-L-R_{7a}$  in which L is a bond or  $SO_2$  and  $R_{7a}$  is substituted or unsubstituted alkyl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 10 -

or substituted or unsubstituted heteroaryl; Z in the iminometal of formula 1' is Cl, Br or I; and the sulfinylimine stereoisomer is a compound of formula



16 (previously presented): A method as claimed in Claim 13, wherein  $R_{12}$  and  $R_{13}$  are both hydrogen.

17 (previously presented): A method as claimed in Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide, 1,2,3-dithiazolidine-S-oxide or 1,2,3-azathiazolidine-S-oxide has been prepared by reacting an optionally N-substituted beta-amino alcohol, thiol or amine with a thionyl halide.

18 (previously presented): A method as claimed in Claim 1, which further comprises the step of alkylating the amine stereoisomer.

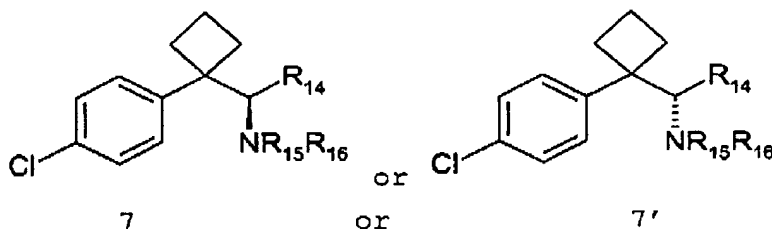
19 (previously presented): A method as claimed in Claim 1, wherein the amine stereoisomer is a compound of formula



Serial No. 10/508,941

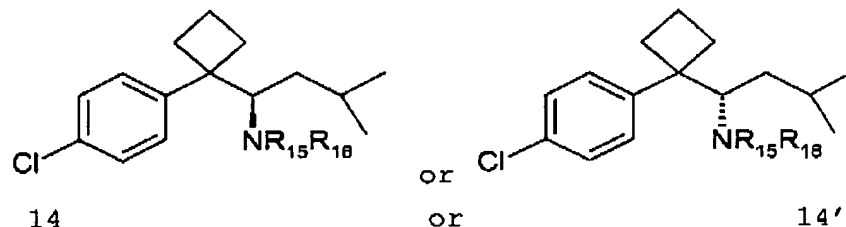
Response to Office Communication of December 15, 2005

- 11 -



or a pharmaceutically acceptable salt, solvate, clathrate, hydrate or prodrug thereof, wherein R<sub>14</sub> is substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl or substituted or unsubstituted aryl, and R<sub>15</sub> and R<sub>16</sub> together with the nitrogen to which they are attached form a heterocycle, or each of R<sub>15</sub> and R<sub>16</sub> is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aralkyl or substituted or unsubstituted aryl.

20 (original): A method as claimed in Claim 19, in which the amine stereoisomer is a compound of formula



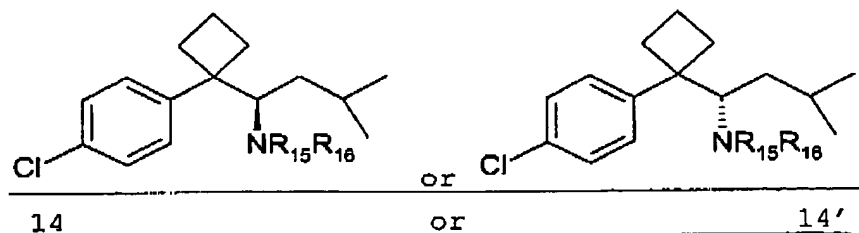
21 (previously presented): A method as claimed in Claim 19, wherein R<sub>15</sub> and R<sub>16</sub> are both hydrogen.

22 (currently amended): A method as claimed in Claim 10 ~~21~~ wherein the amine stereoisomer is a compound of formula

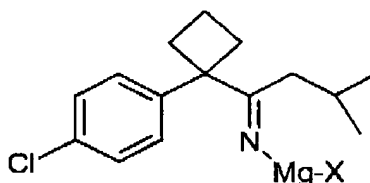
Serial No. 10/508,941

Response to Office Communication of December 15, 2005

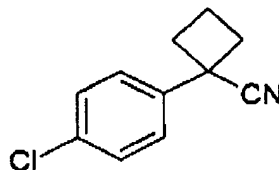
- 12 -



wherein  $R_{15}$  and  $R_{16}$  are both hydrogen and the metal imine is a compound of formula



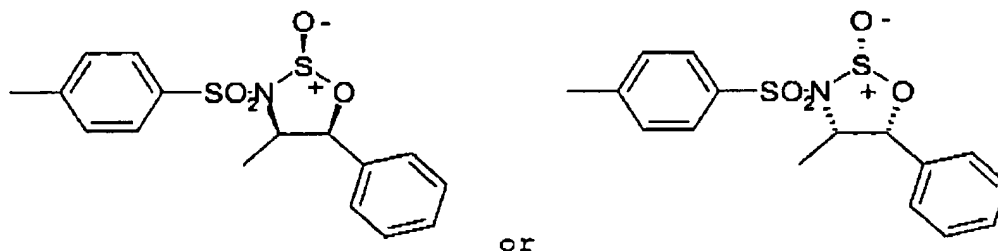
that has been obtained by contacting a compound of formula



15

with a compound of formula  $i\text{-BuMg-X}$  wherein  $X$  is a halogen.

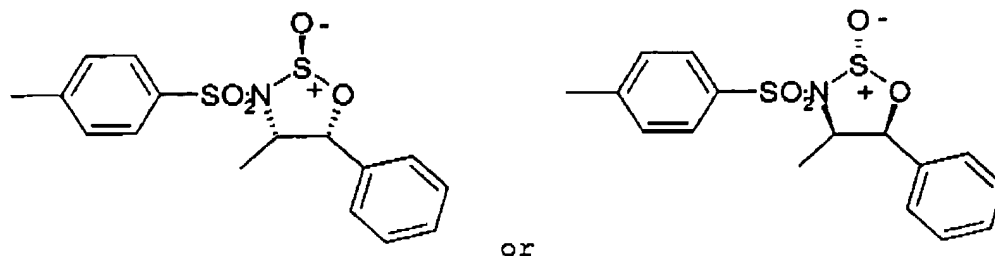
23 (previously presented): A method as claimed in Claim 10, wherein the 1,2,3-oxathiazolidine-S-oxide is a compound of the formula



Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 13 -



24 (previously presented): A method as claimed in Claim 1, wherein the sulfinylimine is reduced using a hydride reducing agent.

25 (original): A method as claimed in Claim 24, wherein the hydride reducing agent is  $\text{NaBH}_4$ .

26 (previously presented): A method as claimed in Claim 1, in which the reagent suitable for the cleavage of a sulfur-nitrogen bond is an acid.

27 (original): A method as claimed in Claim 26 wherein the acid is  $\text{HCl}$ .

28 (previously presented): A method as claimed in Claim 1, in which reaction of the sulfinylamine stereoisomer with the reagent suitable for the cleavage of a sulfur-nitrogen bond also affords an optionally N-substituted beta-aminoalcohol, and this optionally N-substituted beta-aminoalcohol is recovered, converted into 1,2,3-oxathiazolidine-S-oxide and recycled.

29 (previously presented): A method as claimed in Claim 1, wherein the stereoselective reduction of the sulfinylimine is performed using a stereoselective reducing agent.

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 14 -

30 (previously presented): A method as claimed in Claim 1, in which the amine stereoisomer is selected from Alacepril, Benazepril, Benazeprilate, Ceronapril, Cilazapril, Cilazaprilat, Delapril, Enalapril, Enalaprilat, Fasidotril, Fosinopril, Imidapril, Imidaprilat, Libenzapril, Lisinopril, Moexipril, Moexiprilat, Moveltipril, Pentopril, Perindopril, Quinapril, Quinaprilat, Ramipril, Sampatrilat, Spirapril, Spiraprilat, Temocapril, Temocaprilate, Trandolapril, Trandolaprilate, Utibapril, Utibaprilat, Zabicipril, Zabiciprilat, Bucillamine, Penicillamine, Thiamphenicol, Cefprozil, Cephalexin, Cephaloglycin, Cilastatin, Alafosfalin, Ethambutol, Sertraline, Tametraline, Acetylcysteine, Selegiline, Azaserine, Dorzolamide, Colchicine, Dilevalol, Enalapril, Methyldopa, Metaraminol, Acivicin, Melphalan, Ubenimex, Tmsulosin, Tirofiban, Dilevalol, N-dodecyl-N-methylephedrinium, Ofenucine, Tinofedrine, Aceglutamide, 1-ephedrine, levopropylhexedrine, (+)-and (-)-Norephedrine, Phenylpropanolamine, Pseudoephedrine, d-farm, (R)-and (S)-Tamsulosin, Dimepheptanol, Lofentanil, Tilidine hydrochloride (+)-trans, Ciramadol, Enadoline, Lefetamine, Spiradoline, (+)-Etoxadrol, Levoxadrol, (R)-Amphetamine, Clobenzorex, Dexfenfluramine, Dextroamphetamine, Etilamfetamine, Fenfluramine, Levofenfluramine, Phenylpropanolamine, Cetirizine, (R)- and (S)-Baclofen, (R)- and (S)-Sibutramine, and pharmaceutically acceptable salts thereof.

31 (withdrawn - currently amended): A method as claimed in Claim 1, wherein the sulfinylimine ~~sulfinylamine~~ stereoisomer is reacted with a source of a nucleophile selected from a nitrile, a Grignard reagent and an organolithium.

Serial No. 10/508,941

Response to Office Communication of December 15, 2005

- 15 -

32 (withdrawn - currently amended): A method as claimed in Claim 31, wherein the sulfinylimine ~~sulfinylamine~~-stereoisomer is reacted with a nitrile, and the resultant amine stereoisomer bearing a nitrile group is hydrolyzed to afford an amino acid.

33 to 45: (cancelled)